# Drug Safety Update

## Latest advice for medicines users

The monthly newsletter from the **Medicines and Healthcare products Regulatory Agency** and its independent advisor the **Commission on Human Medicines**

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**The Medicines and Healthcare products Regulatory Agency** is the government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe.

**The Commission on Human Medicines** gives independent advice to ministers about the safety, quality, and efficacy of medicines. The Commission is supported in its work by Expert Advisory Groups that cover various therapeutic areas of medicine.

Cases of accidental overdose have been reported during treatment with intravenous paracetamol 10 mg/mL solution for infusion (Perfalgan ▼). In most cases, this occurred in infants and neonates due to confusion between the prescription of Perfalgan being issued in mg and then administered in mL; in most of these cases, a 10-fold overdose was reported. Read our advice to help minimise the risk of accidental overdose; this includes a reminder on recommended doses depending on patient weight (p 2).

Also this month, we remind you about the withdrawal of orciprenaline sulphate (a non-specific β-agonist for reversible airway obstruction) from the UK market on Sept 30, 2010 (p 5).

Finally, we have news that information for patients about the Yellow Card Scheme has been made available in 11 languages in addition to English (p 4).

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# Drug safety advice

## Intravenous paracetamol (Perfalgan ▼): risk of accidental overdose, especially in infants and neonates

**Keywords:** intravenous paracetamol, Perfalgan (▼)

**Vigilance is advised when prescribing and administering intravenous paracetamol 10 mg/mL solution for infusion (Perfalgan ▼) to ensure that the correct dose is given. For all patients, dose requirement is based on weight as outlined below and in the product information. For infants and children who weigh less than 33 kg, the 50 mL vial should be used for administration**

Cases of accidental overdose have been reported during treatment with intravenous paracetamol 10 mg/mL solution for infusion (Perfalgan ▼). In most cases, this occurred in infants and neonates due to confusion between the prescription of Perfalgan being issued in mg and then administered in mL; in most of these cases, a 10-fold overdose was reported.

Perfalgan is indicated for the short-term treatment of pain and fever, when there is a clinical need of paracetamol administration intravenously. It is available as a solution for infusion of 10 mg paracetamol per 1 mL solution in 50 mL vials and 100 mL vials. The 50 mL vial is only for use in term newborn infants, infants, toddlers, and children who weigh less than 33 kg.

The recommended dose of Perfalgan depends on the weight of the patient, and is summarised in the table below.

**Note** that irrespective of dose, the dosing schedule is up to four infusions a day with a minimum of 4 hours between each administration (6 hours for those with renal impairment).

| | **Term newborn infants, infants, toddlers, and children weighing <10 kg** | **Children weighing >10 kg and <33 kg** | **Children, adolescents, and adults weighing >33 kg and <50 kg** | **Adolescents and adults weighing >50 kg** |
|---|---|---|---|---|
| **Dose (per administration)** | One intravenous infusion of 7·5 mg/kg: **ie, 0·75 mL solution per kg** | One intravenous infusion of 15 mg/kg: **ie, 1·5 mL solution per kg** | One intravenous infusion of 15 mg/kg: **ie, 1·5 mL solution per kg** | One intravenous infusion of 1 g: **ie, 100 mL solution** |
| **Maximum daily dose** | **30 mg/kg (ie, 3 mL/kg)** | 60 mg/kg **(ie, 6 mL/kg)** without exceeding 2 g **(ie, 200 mL)** in total | 60 mg/kg **(ie, 6 mL/kg)** without exceeding 3 g **(ie, 300 mL)** in total | Must not exceed 4 g **(ie, 400 mL)** in total |

**Note:** maximum daily dose in each dose range refers to that for maximum weight in each range.

Further information can be found in a letter to healthcare professionals sent May 2010, see http://www.mhra.gov.uk/Safetyinformation/Safetywarningsalertsandrecalls/Safetywarningsandmessagesformedicines/Monthlylistsofinformationforhealthcareprofessionalsonthesafetyofmedicines/CON084656

### Infants and children

Up to May 31 2010, 23 cases of accidental overdose with Perfalgan have been reported worldwide in children younger than 1 year, one of which was fatal. In the UK, there have been seven reports of overdose in infants and neonates. In most of these cases, a 10-fold overdose was reported.

A dosing table for infants and children of different weights is provided below:

| Paracetamol dose (mg/kg) | Weight (kg) | Calculated dose (mg) | Volume of solution (mL) |
|---|---|---|---|
| **Infants and children weighing ≤10 kg** | | | |
| 7·5 | 3 | 22·5 | 2·25 |
| | 5 | 37·5 | 3·75 |
| | 7 | 52·5 | 5·25 |
| | 10 | 75 | 7·5 |
| **Children weighing >10 kg** | | | |
| 15 | 15 | 225 | 22·5 |
| | 20 | 300 | 30 |
| | 30 | 450 | 45 |

**Advice for healthcare professionals:**

- Vigilance is advised when prescribing and administering Perfalgan to ensure that the correct dose is given, especially in infants and neonates where there is a risk of confusion due to prescription in mg and administration in mL
- For all patients on the basis of their weight, adhere to the recommended dose as outlined above and in the product information; the dosing schedule is up to four infusions a day with a minimum of 4 hours between each administration, 6 hours for those with renal impairment
- For infants and children who weigh less than 33 kg, the 50 mL vial should be used
- In order to avoid overdose, intravenous paracetamol should not be given concomitantly with oral paracetamol, including combination products

### Reporting of suspected adverse reactions

Perfalgan is under intensive monitoring (▼) by the MHRA, and healthcare professionals are reminded to report all suspected adverse reactions promptly via the Yellow Card Scheme (see www.yellowcard.gov.uk).

# Yellow Card Scheme update

The Yellow Card Scheme collects information on suspected adverse drug reactions. See www.yellowcard.gov.uk

## Information is now available in a number of languages

Information for patients about the Yellow Card Scheme has been made available in 11 languages in addition to English. These languages are:

- Arabic
- Bengali
- Chinese (simplified)
- Czech
- Polish
- Portuguese
- Punjabi
- Russian
- Slovakian
- Urdu
- Welsh

Please tell your patients that they can access information about the Yellow Card Scheme in the above languages. Copies of the leaflets can be downloaded from the Yellow Card website at: http://yellowcard.mhra.gov.uk/information-in-other-languages/.

A range of other leaflets, information cards, and posters are also available to download at http://yellowcard.mhra.gov.uk/downloads/. We can provide hard copies of some of these—please contact 0800 731 6789 to make a request.

# Stop press

## Orciprenaline sulphate (Alupent): reminder of withdrawal from the market on Sept 30, 2010

*Please ensure that patients are transferred to alternative bronchodilator therapy.*

For further information see http://www.mhra.gov.uk/Safetyinformation/Safetywarningsalertsandrecalls/Safetywarningsandmessagesformedicines/CON062529

**Orciprenaline sulphate** (Alupent syrup), a non-specific β-agonist, was formerly licensed for reversible airway obstruction and suggested for maintenance therapy. It is to be withdrawn from the UK market on Sept 30, 2010. A comprehensive analysis of the available literature was completed last year, which showed that it was significantly less efficacious than other more-specific $\beta_2$ agonists and was associated with a higher incidence of side effects. The review concluded that the risk-benefit balance was unfavourable. Accordingly, the Commission on Human Medicines concluded that there:

- should be a planned withdrawal of orciprenaline sulphate from the UK market
- are no patient groups for whom transfer to a more-selective $\beta_2$-agonist would be inappropriate

Orciprenaline sulphate will no longer be available after Sept 30, 2010. All patients who are currently receiving this medicine should be switched to a more-selective short-acting $\beta_2$-agonist such as salbutamol or terbutaline as soon as possible.

# Other information from the MHRA

## Patient Information Leaflet of the month: medicines used in mental health

Patient Information Leaflets (PILs) are improving in quality as a result of new legal obligations on manufacturers to test the documents with potential patients. Testing makes sure that the presentation of the information enables patients to find and understand key messages for supporting safer use of the medicine within the PIL and thereby enables them to use the medicine safely and effectively. To promote this initiative, we are publishing a series of examples of best practice on our website. The latest examples in the series are leaflets which accompany various medicines used in the specialty of mental health. The leaflets have recently been redesigned to clarify the key information and use good navigation tools. In testing the leaflets were well received by patients.

The examples of leaflets in this feature can be found at: http://www.mhra.gov.uk/Howweregulate/Medicines/Labelspatientinformationleafletsandpackaging/Patientinformationleaflet(PIL)ofthemonth/index.htm

**Read more about the Commission on Human Medicines, including summaries of minutes from meetings, at www.mhra.gov.uk/Committees/Medicinesadvisorybodies/CommissiononHumanMedicines/index.htm**

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